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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/694,758	10/23/2000	Shukti Chakravarti	021825-004710US	7408
20350 7590 02/19/2008 TOWNSEND AND TOWNSEND AND CREW, LLP TWO EMBARCADERO CENTER EIGHTH FLOOR SAN FRANCISCO, CA 94111-3834			EXAMINER LIU, SUE XU	
			ART UNIT 1639	PAPER NUMBER
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

09/694,758

**Applicant(s)**

CHAKRAVARTI, SHUKTI

**Examiner**

Sue Liu

**Art Unit**

1639

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 November 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 42 and 45-56 is/are pending in the application.
- 4a) Of the above claim(s) 46, 53, 55 and 56 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 42, 45, 47-52 and 54 is/are rejected.
- 7) ☒ Claim(s) 42 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-884)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_
- Paper No(s)/Mail Date \_\_\_\_\_

## **DETAILED ACTION**

### ***Claim Status***

1. Claims 1-41, 43 and 44 have been canceled as filed on 11/30/07.  
Claims 53-56 have been added as filed on 11/30/07.  
Claims 42 and 45-56 are currently pending  
Claims 46, 53, 55 and 56 have been withdrawn.  
Claims 42, 45, 47-52 and 54 are being examined in this application.

### ***Election/Restrictions***

2. Applicants elected Group IV (original Claims 5-7), and MMP-12 for the species of a gene (Reply filed on 5/16/02), as acknowledged in the previous Office action mailed 7/30/02, p. 2. The instant claim 46 has been amended to recite GRO3 gene (as filed on 11/30/07), which the GRO3 gene is distinct from the originally elected species "MMP-12" gene. Thus, the instant claim 46 is withdrawn due to non-elected species.
3. Applicants have added new claims 53-56 reciting non-elected species. The newly added claims 53, 55 and 56 recites HNL gene, elafin gene, and COL6A3 gene that are distinct from the elected species "MMP-12" gene. Thus, claims 53, 55 and 56 are withdrawn due to non-elected species.

***Priority***

4. This application claims priority to U.S. Provisional Patent Application No. 60/160,835, filed 10/21/1999.

***Specification***

**Sequence Rule Compliance**

5. Applicant's submission of the new Sequence Listing as filed on 11/30/07 is acknowledged.

**Claim Rejections Withdrawn**

6. In light of applicants' amendment to the claims, the following rejection is withdrawn:
- A.) Claims 42-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. (Written Description Rejection).
- B.) Claims 42-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. (New Matter Rejection).
7. Upon further consideration, the following claim rejections are withdrawn:
- A.) Claims 42-44, 46-48, and 50-52 are rejected under **35 U.S.C. 102(e)** as being anticipated by Cocks et al (US 6,607,879; 08/19/2003; Filed on 2/9/1998).
- B.) Claims 42-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cocks et al (US 6,607,879; 08/19/2003; Filed on 2/9/1998), in view of Alexander et al (Digestive

Diseases and Sciences, Vol. 41, No. 4 (April 1996), pp. 660-669; previously cited) and Dieckgraefe et al (Gastroenterology, vol 114, No. 4, April 1998; cited previously).

**Maintained Claim Rejections**

***Claim Rejections - 35 USC § 112***

**Second paragraph of 35 U.S.C. 112**

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 42, 45, 47-52 and 54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The previous rejection over claims 42, 45 and 47-52 is maintained for the reasons of record as set forth in the previous Office action. The rejection over claims 43, 44 and 46 is moot due to applicant's cancellation of and amendments to the said claims. The rejection over claim 54 is necessitated by applicant's amendment to the claims.

Claim 42 appears to recite alternative limitations in steps (or parts) (a)-(e) of the claim. However, the listed steps/parts are not clearly recited in alternative format. It is not clear the "expression level" is the combination of expression level profiles from all the recited genes in step (a), or if the expression level is each one of the gene product. Applicants are respectively directed to MPEP 2173.05 (h) for guidance in alternative limitations.

Claim 42 also recites in part (g): "associating an increase in the expression level of... said MMP-12 gene... with a UC phenotype in said test colon cell", and in part (h): "associating an

increase in the expression level of said MMP-12 gene... with a CD phenotype in said test colon cell” (emphasis added). The said claim seems to recite that an increase in MMP-12 gene expression indicate a “UC phenotype” as well as a “CD phenotype”. Thus, it is not clear if an increase in MMP-12 is indicative of both type of diseases or either one of the said diseases. In the preamble of the instant claim 42, the claimed method is recited to have the intended use of “determining whether a test colon cell has an ulcerative colitis (UC) or Crohn’s disease (CD) phenotype”, which recitation can be interpreted to mean “distinguishing between UC or CD” based on gene expression. However, if the MMP-12 gene is overexpressed in both CD and US, a distinction cannot be made, and thus the instant claim language is in conflict.

Claim 45 recites “distinguishing between a UC or CD phenotype in said test colon cell”, which is unclear. It is not clear if the instant claim language is reciting a comparing between the UC and the CD phenotype, or if the claim is reciting a determination of each of the UC or CD phenotype individually.

Discussion and Answer to Argument

10. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant’s traversal is addressed below (applicant’s arguments are in italic):

*Applicants assert the current claim amendment overcomes the previous rejection because the claim recite “GRO3, HNL, MMP-12, elafin, and COL6A3”. (Reply, pp. 10-11).*

However, the instant claim 42 as amended does not recite the specific combination of genes as asserted by applicants. The instant claim as amended is unclear and does not recite the conjunction, "and".

In addition, the claim amendments also elicit new issues under 35 USC 112, 2<sup>nd</sup> paragraph. Applicants are respectively directed to the above rejection for detailed discussion of the said issues.

### ***Claim Rejections - 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

#### **Alexander and Poulakkainen**

13. Claims 42, 45, 47, 48, 50-52 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alexander et al (Digestive Diseases and Sciences, Vol. 41, No. 4 (April 1996), pp. 660-669; previously cited), and Poulakkainen (Gastroenterology. 114:A1064; 1998; previously cited). The previous rejection over claims 42, 45, 47, 48 and 50-52 is maintained for

the reasons of record as set forth in the previous Office action. The rejection over claims 43, 44 and 46 is moot due to applicant's cancellation of and amendments to the said claims. The rejection over claim 54 is necessitated by applicant's amendment to the claims.

**Alexander** et al, throughout the publication, disclose a method to determine altered expression of protooncogenes (cell cycle related genes) in patients with inflammatory bowel disease (IBD), which reads on the determining gene expression of **clm 42**. The reference assayed transcripts of 15 protooncogenes (refer to IBD genes) in colonic epithelial cells of IBD patients and controls (e.g., see abstract). The reference discloses that increased levels (refers to the differential expression of the instant claim) of soluble mediators (e.g. Leukotrienes, prostaglandins) of inflammation as well as the cells of immune system have been found to be present in the intestinal mucosa and submucosa of IBD patients (e.g., see page 660, last paragraph bridging first paragraph in page 661). The reference discloses expression of transcripts of eight growth factor receptor related genes in colonic epithelial cells of IBD patients and controls (i.e., see left column in page 661). These read on the comparison step of **clm 42**.

The reference discloses that the level of expression of *c-fos* in the involved IBD samples was about two fold higher than in the uninvolved IBD samples, which reads on the at least a factor of two difference in expression level of **clm 54**. The reference also teaches cells obtained from patients with UC and CD (Abstract of the reference), which reads on UC or CD test cells of **clm 42**. The reference also teaches that certain genes expression levels are different in UC when compared to CD patients (Abstract of the reference), which reads on the distinguishing between UC and CD step of **clm 45**.



The reference also teaches samples are obtained from surgery (p. 661, right col., para 2), which reads on the sample of **clm 47**. The reference also teaches hybridization analysis (e.g. northern blotting) to analyze gene expression (p. 662, right col.), which reads on the method step of **clm 48**. The northern blotting membrane also reads on an array having a substrate (**clms 49-52**), because the northern blotting membrane has probes bound thereto and the probes are arranged in a two dimensional matrix format (see Figure 2 of the reference).

Overall, Alexander et al teach a method to determine the differential expression of genes involved in IBD.

Alexander et al do not explicitly teach the listed genes in the instant **clm 42**. However, the genes (such MMP-12) in listed in the instant Claim 42 (and Table 1 of the instant specification) are not novel genes, and are well known for their role in IBD. The specification in page 19, discloses 'Table 1 indicates those sequences which are over- or underexpressed in a CD- or UC-derived cells relative to normal tissue.' Applicants in the specification disclose the GenBank accession numbers of the genes used in the claimed method. Thus, all the genes used in the claimed method are well known in the art.

**Puolakkainen** et al (G4358), throughout the publication, teach distinct expression profiles of stromelysin-s, collagenase and MMP-12 in intestinal ulcerations. As taught by Alexander et al, Crohn's disease (CD), and ulcerative colitis (UC) are part of larger group of IBDs (p. 660 of Alexander). The Puolakkainen reference also teaches the MMP-12 gene is "abundantly expressed" in test tissues when compared to normal tissues, which "abundant expression" read on the inherent property of the MMP-12 gene differential expression pattern (with at least a factor of two increase in expression).

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use all the known genes (such as MMP-12) involved in IBD or its subtypes (such as UC or CD) and use the genes (or probes) in array format to determine the IBD or pre-IBD phenotype.

A person of ordinary skill in the art would have been motivated to use all the known genes or genetic markers (such as MMP-12) involved in IBD (or its subtypes including CD and UC) in an array format to screen IBD cells, such that the efficiency of the method improves (i.e., more markers used the more different mechanisms involved in IBD are determined). Because Alexander et al teach that the genes that are differentially expressed in IBD patients can be used as markers for development of colon cancer in IBD (Abstract, last lines), a person of ordinary skill in the art would have been motivated at the time of the invention was made to use the differentially expressed MMP-12 (as taught by Puolakkainen et al) as a gene marker for determining IBD phenotype of cells.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications because the techniques for monitoring gene expression such as using DNA microarray and the specific genes (such as MMP-12) are known in the prior art such as taught by Alexander et al and Puolakkainen et al, who have demonstrated the detection of expression of various genes in IBD cells.

Discussion and Answer to Argument

14. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

*Applicants argue that each of the cited references individually does not teach all element of the claimed invention (Reply, pp. 13+). Applicants specifically argue that the combination of references does not teach all "five genes" (i.e. GRO3, HNL, MMP-12, elafin, and COL6A3) listed in the instant claim 42 (Reply, pp. 13+).*

First, the instant claim language does not require all five listed genes for the claimed method. The instant claim 42 recites the following:

"A method for determining whether a test colon cell has an ulcerative colitis (UC) or Crohn's disease (CD) phenotype, said method comprising:

(a) determining an expression level of a macrophage inflammatory protein-2 $\beta$  (GRO3) gene product in said test colon cell;

(b) determining an expression level of a ...(HNL)...

(c) determining an expression level of a ...(MMP-12)...

(d) determining an expression level of a ...(elafin)...

(e) determining an expression level of a ...(COL6A3)...

(f) comparing the expression level of each of said gene products in said test colon cell to an expression level of the same gene product in a normal colon cell;

(g) associating an increase in the expression level of said GRO3 gene product, said HNL gene product, said MMP-12 gene product, said elafin gene product, or said COL6A3 gene product in said test colon cell relative...

(h) associating an increase in the expression level of said MMP-12 gene product or said elafin gene product..." (emphasis added).

The instant claim language as amended is not clear as drawn to a combination of genes OR to alternative genes. Applicants have deleted the conjunction in between part (d) and (e) of the instant claim 42. It appears that the instant claim 42 is reciting the claimed "genes" in the alternative (i.e. "or"). This interpretation of the claim is supported by the alternative recitation in part (g) and (h) of the instant claim. The instant claim 42 recites determining the gene expression level in any one of the listed five alternative genes in part (g) and (h).

Applicants are respectively directed to MPEP 2173.05(h) for proper alternative language when drafting Markush type of group.

See also MPEP 2131 and 2131.02 for discussion of species anticipating a genus:

"'When a claim covers several structures or compositions, either generically or as alternatives, the claim is deemed anticipated if any of the structures or compositions within the scope of the claim is known in the prior art.' Brown v. 3M, 265 F.3d 1349, 1351, 60 USPQ2d 1375, 1376 (Fed. Cir. 2001)" (MPEP 2131)

In this case, the instant claim language (claim 42) can be interpreted to recite alternative methods of determining expression level of the different genes listed in the alternative. Thus, as

long as the cited reference teaches one of the “alternatives” (or genes), the cited reference anticipates or renders obvious of the entire claim.

*Applicants also assert it is improper to use the instant specification for the above rejection. (Reply, p.13).*

However, the teachings relied upon for every element of the instant claims are not gleaned from the instant specification. The instant specification was only cited to illustrate the admitted fact that the instant claimed genes (and their sequences) are known in the prior art.

*Applicants also argue the Poulakkainen reference fails to teach “determining whether a test colon cell has a UC or CD phenotype comprising determining the expression level of each of the five claimed gene products in the test colon cell” (Reply. p.14).*

First, the above said feature is not clearly claimed in the instant claim. The instant claim does not teach using the gene expression profile of the combination of the listed five genes to determine the UC or CD phenotype. The instant claim only seems to recite the genes in the alternative. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., “*determining whether a test colon cell has a UC or CD phenotype comprising determining the expression level of each of the five claimed gene products in the test colon cell*”) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Second, applicants have only argued that one of the cited references does not teach the above said feature. However, the above rejection is over a combination of references. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

*Dieckgraefe and Poulakkainen*

15. Claims 42, 45, 47-52 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dieckgraefe et al (Gastroenterology, vol 114, No. 4, April 1998; cited previously) and Poulakkainen (G4358; cited previously). The previous rejection over claims 42, 45 and 47-52 is maintained for the reasons of record as set forth in the previous Office action. The rejection over claims 43, 44 and 46 is moot due to applicant's cancellation of and amendments to the said claims. The rejection over claim 54 is necessitated by applicant's amendment to the claims.

**Dieckgraefe** et al, throughout the publication, disclose a method for identifying gene expressed in IBD, which reads on the determining gene expression of **clm 42**. The reference has used GeneChip expression monitoring system to examine mucosal gene expression in ulcerative colitis, Crohns' disease, and both in inflamed and non-inflamed non IBD specimens (Background section of the reference), which reads on the UC and DC of **clm 42**. The reference also teaches RNA isolated from the mucosa of colonic resection specimens was used to generate hybridization probes (See Methods), which reads on the surgical resection sample of **clm 47**. The

reference also teaches light directed solid-phase combinatorial chemistry was used to generate oligonucleotide probe array (see Methods), which reads on the nucleic acid probes, array, and substrates of **clms 48-52**. The reference in the results section discloses that dramatic changes were seen in the expression of wide range of genes, genes were identified which appear to be specific markers for the specific diagnosis, disease activity and specific feature of histology, and specific genotype diagnosis for UC group, which read on the step of distinguishing between UC and CD of **clm 45**. The reference also teaches dramatic changes of gene expression for a wide range of genes (Results section of the reference), which reads on the at least a factor of two difference in expression of **clm 46**.

Dickgraefe et al also teach the need to identify gene markers differentially expressed in CD and UC, and the need to use different genes that are differentially expressed to identify genotypes for the different diseases (such as CD and UC) for potential pharmaceutical purposes (see Aims section of the reference). The reference further teaches host defense molecules are over expressed in IBD cells (Results section).

Dickgraefe et al do not explicitly teach using MMP-12 as a gene marker for IBD determination.

However, the genes shown in Table 1 (which comprises MMP-12) of the instant specification are publicly known and available. Furthermore, **Puolakkainen** et al, throughout the publication, teach distinct expression profiles of stromelysin-s, collagenase and MMP-12 in intestinal ulcerations. The Puolakkainen reference also teaches the MMP-12 gene is “abundantly expressed” in test tissues when compared to normal tissues, which “abundant expression” read

on the inherent property of the MMP-12 gene differential expression pattern (with at least a factor of two increase in expression).

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention to use all the known genes involved in IBD and use the genes (or probes) in array format to determine the IBD or pre-IBD phenotype.

A person of ordinary skill in the art would have been motivated to use all the known genes or genetic markers involved in IBD in an array format to screen IBD cells, such that the efficiency of the method improves (i.e., more markers used the more different mechanisms involved in IBD are determined). Because Dieckgraefe et al teach the need to identify gene markers differentially expressed in different diseases such as UC and CD for potential pharmaceutical purposes, and many host defense molecules are over expressed in IBD cells, a person of ordinary skill in the art would have been motivated at the time of the invention was made to use the differentially expressed MMP-12 (as taught by Puolakkainen et al) as a gene marker for determining IBD phenotype of cells.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications because the techniques for monitoring gene expression such as using DNA microarray and the specific genes (such as MMP-12) are known in the prior art such as taught by Dieckgraefe et al and Puolakkainen et al, who have demonstrated the detection of expression of various genes in IBD cells.



*Discussion and Answer to Argument*

16. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants traversed the above rejection with the same argument as the traversal over the rejection using the combination of the Alexander and Poulakkainen references. Thus, applicants are respectively directed to the discussion under the "Alexander and Poulakkainen" rejection for answer to arguments.

*Alexander and others*

17. Claims 42, 45, 47-52 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alexander et al (Digestive Diseases and Sciences, Vol. 41, No. 4 (April 1996), pp. 660-669; previously cited), in view of Poulakkainen (G4358; previously cited) and Dieckgraefe et al (Gastroenterology, vol 114, No. 4, April 1998; cited previously). The previous rejection over claims 42, 45 and 47-52 is maintained for the reasons of record as set forth in the previous Office action. The rejection over claims 43, 44 and 46 is moot due to applicant's cancellation of and amendments to the said claims. The rejection over claim 54 is necessitated by applicant's amendment to the claims.

The combination of Alexander and Poulakkainen references teaches using various gene expression in cells from patients with IBD, as discussed above.

The combination of said references does not expressly teach using probes with length of 12-40 nucleotides as recited **clm 49**.

**Dieckgraefe** et al (G4358), throughout the publication, teach using probes with length of 25 nucleotides.

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use probes with specific length to detect gene expression product.

A person of ordinary skill in the art would have been motivated to use probes with specific length to detect gene expression, because probes with different lengths are known in the art and they can be used to represent diverse genes, as taught by Dieckgraefe et al.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications because the techniques for generating probes with certain length is known in the art, as evidenced by Dieckgraefe et al.

*Discussion and Answer to Argument*

18. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants traversed the above rejection with the same argument as the traversal over the rejection using the combination of the Alexander and Poulakkainen references. Thus, applicants are respectively directed to the discussion under the "Alexander and Poulakkainen" rejection for answer to arguments.

**New Claim Objection(s) / Rejection(s)**

***Claim Objections***

19. Claim 42 is objected to because of the following informalities: The instant claim 42 is missing a proper conjunction (i.e. "and" or "or") in between part (d) and (e) of the said claim. Appropriate correction is required.

***Conclusion***

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

Application/Control Number:  
09/694,758  
Art Unit: 1639

Page 19

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SL/  
Art Unit 1639  
2/4/08

/Jon D. Epperson/  
Primary Examiner, AU 1639